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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/885,259 | 02/23/2001 | Madhav N. Devalaraja | PC18174A | 3713 |

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| EXAMINER | |
|---|---|
| BELYAVSKYI, MICHAIL A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/885,259 | DEVALARAJA ET AL. | |
| | Examiner | Art Unit | |
| | Michail A. Belyavskyi | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *34, 36 and 48 -53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34, 36 and 48 -53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/29/05 has been entered.

2. Claims 34, 36 and 48 -53 are pending and under consideration in the instant application.

In view of the amendment, filed 06/29/05 the following rejections remain:

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 34, 36 and 48 –53 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,837,460 in view of newly submitted Janeway et al. ( Immunobiology, Third Edition, 1999, pages 650-651 ) for the same reasons set forth in the Office Action mailed on 04/08/05.

Applicant's argument filled on 06/29/05 have been fully considered but have not been find convincing.

Applicant asserts that presently amended claims all require that M-CSF antibody inhibit the synergistic effect of M-CSF on MPC-1 mediated shape change. US Patent '460 does not disclosed that M-CSF antibody inhibit the synergistic effect of M-CSF on MPC-1 mediated shape change.

It appears that applicant relies upon an asserted and claimed mechanism of action but does not provide objective evidence that the prior art teaching of treating the same patient populations with active immunization that will result in producing M-CSF antibody in mammals to achieve the same therapeutic effect differs from the claimed methods. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which a M-CSF antibody treating rheumatoid arthritis in mammal it does not appear to distinguish the prior art teaching nearly the same methods to achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

US Patent '460 teaches a method for ameliorating the effects of inflammation in a mammal , comprising administering to said mammal a therapeutically effective amount of an M-CSF or GM-CSF antigen or antibody to M-CSF or GM-CSF antibody. ( see entire document, Abstract and columns 5 and 9 in particular). In other words, US Patent ' 460 teaches a method for treating inflammation in a mammal using method of active immunization with M-CSF or GM-CSF antigen.

US Patent '460 does not explicitly teaches a method for ameliorating the effects of inflammation in a mammal comprising administering to said animal a therapeutically effective amount of antibody to M-CSF, i.e passive immunization.

Janeway et al. teach that it is well known that treating diseases can be done by either passive immunization i.e. by administering to a patient an antiserum or purified antibodies specific for an antigen or by active immunization, i.e. by administering to a patient an antigen that will result in production of antigen-specific antibodies. Janeway et al. teach that passive immunization provides protection against many pathogens and should be used when immediate protection is required. ( see pages 650-651 in particular).

It is noted that the reference method uses a method of active immunization ( administering M-SCF antigen to the patient) while the claimed method uses the method of passive immunization ( administering antibody to a M-CSF to the patient) to achieve the same results. It is clear that both the prior art and applicant administer the similar treatment, i.e. active and passive immunization against M-CSF to the same patient to achieve the same results, i.e. to treat rheumatoid arthritis. Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to apply teaching of Janeway et al., to those of US Patent '460 and substitute active immunization with M-CSF antigen or anti-antibody to M-CSF with passive immunization with antibody M-CSF.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because both method of active and passive immunization were well known to one skilled in the art at the time the invention was made and were widely used to treat diseases as taught by Janeway et al. Thus passive immunization can be used instead of active immunization in the method of treating rheumatoid arthritis taught by US Patent '460.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. Claims 34, 36 and 48 -53 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/09561 in view of Campbell et al., (1998, IDS) as is evidence from Campbell et al (2000, IDS) for the same reasons set forth in the Office Action mailed on 04/08/05.

Applicant's argument filled on 06/29/05 have been fully considered but have not been find convincing.

Applicant asserts that presently amended claims all require that M-CSF antibody inhibit the synergistic effect of M-CSF on MPC-1 mediated shape change. There is no disclosure in prior art references that M-CSF antibody inhibit the synergistic effect of M-CSF on MPC-1 mediated shape change.

It appears that applicant relies upon an asserted and claimed mechanism of action. However, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which a M-CSF antibody treating rheumatoid arthritis in mammal it does not appear to distinguish the prior art teaching nearly the same methods to achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which

is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.
WO'561 teaches a method for ameliorating the effects of inflammation in a subject including rheumatoid arthritis, comprising administering an antibodies against GM-CSF, ( see entire document, Abstract and overlapping pages 6-7 in particular). WO'561 teaches that said antibody is monoclonal antibody or human antibody ( see page 6 in particular).

WO'561 does not explicitly teach a method for ameliorating the effects of inflammation in a subject including rheumatoid arthritis, comprising administering an antibodies against M-CSF

Campbell et al., (1998) teaches that there is increasing evidence that the colony-stimulating factors (CSFs) play a part in chronic inflammatory autoimmune diseases such as rheumatoid arthritis. It is noted that although Campbell et at., (1998) does not explicitly disclosed M-CSF, it referenced to the general knowledge of one skilled in the art , by citing Metcalt et a.l and Hamilton et al references ( see pages 3639, 3643 and 3644 in particular). The combined references teach that colony- stimulating factors (CSF) are a family of four cytokine growth factors including macrophage CSF ( M-CSF) and granulocyte-marcophage CSF (GM-CSF) each known to exhibit certain activities that predispose them towards a proinflammatory role *in vivo*. Moreover, the fact that said general knowledge was well known to one skilled in the art at the time the invention was made is evidenced from the second Campbell et al. reference (2000, IDS). In the second reference, Campbell et al., explicitly stated that combined references of Metcalt et a., l(1991) and Hamilton et al., (1980) teaches that colony- stimulating factors (CSF) are a family of four cytokine growth factors including macrophage CSF ( M-CSF) and granulocyte-marcophage CSF (GM-CSF) each known to exhibit certain activities that predispose them towards a proinflammatory role *in vivo*. ( see page 144 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Campbell et al., (1998) to those of WO' 561 to obtain a claimed method for treating rheumatoid arthritis in a mammal comprising administering an antibody to a M-CSF.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because colony- stimulating factors (CSF) are a family of four cytokine growth factors including macrophage CSF ( M-CSF) and granulocyte-marcophage CSF (GM-CSF) each known to exhibit certain activities that predispose them towards a proinflammatory role *in vivo and* play a part in chronic inflammatory autoimmune diseases such as rheumatoid arthritis. as taught by Campbell et al. Thus the antibody to one member of the family, i.e. GM-SCF can be substituted with antibody to the other member of the family, i.e. M-CSF in the method of treating rheumatoid arthritis in patients taught by WO 00/09561.

The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144. From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The following new ground of rejection is necessitated by the amendment filed 06/29/05.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

7. Claims 34, 36 and 48 -53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" wherein said antibody inhibits the synergistic effect of M-CSF on MCP-1 mediated monocytes shape change" claimed in claims 34, 50, 51, 52 and 53 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally field only support " A method of treating rheumatoid arthritis in a mammal comprising administering a therapeutically effective amount of an antibody to M-CSF".

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 19, 2005